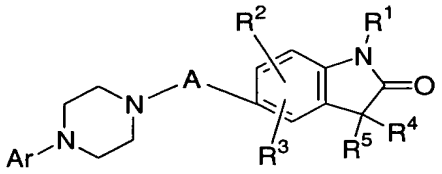
CLAIMS

1. The present invention relates to compounds of the formula **I**



I

wherein Ar is 1,2-benzisothiazoyl, 1,2-benzisothiazoyl-1-oxide, 1,2-benzisothiazoyl-1-dioxide, 1,2-benzisoxazoyl, naphthyl, pyridyl, quinolyl, isoquinolyl, benzothiadiazolyl, benzotriazolyl, benzoxazolyl, benzoxazolonyl, phthalazinyl, indolyl, indanyl, 1H-indazoyl, or 3-indazolyl, and wherein Ar can optionally be substituted by one or more substituents, preferably from zero to three substituents, independently selected from halo, preferably chloro or fluoro, cyano, nitro, (C_1-C_6) alkyl optionally substituted with from one to three fluorine atoms and (C_1-C_6) alkoxy optionally substituted with from one to three fluorine atoms; with the proviso that Ar can not be attached to the piperizine ring via a phenyl ring of Ar;

A is -$(CH_2)_nCH_2$-, wherein n is an integer from one to three, wherein one of the CH_2 groups of A that is not adjacent to the piperizine nitrogen can optionally be replaced by an oxygen atom or by NR, wherein R is (C_1-C_6) alkyl, and wherein one of the carbon atoms of A can optionally be substituted by oxo, amino, NHR wherein R is hydroxy or (C_1-C_6) alkyl, and wherein each R group in a compound of the formula **I** is independent of any other R group in such compound;

R^2 and R^3 are independently selected from hydrogen, (C_1-C_6) alkyl optionally substituted with from one to three fluorine atoms, (C_1-C_6) alkoxy

optionally substituted with from one to three fluorine atoms, (C_2-C_6) alkenyl optionally substituted with from one to three fluorine atoms, (C_2-C_6) alkenoxy optionally substituted with from one to three fluorine atoms, -C(C=O)-(C_1-C_6)alkyl, -C(C=O)-(C_1-C_6)alkenyl having one or two sites of unsaturation, halogen, nitro, cyano, hydroxy, amino, (C_1-C_6) alkylamino, di-(C_1-C_6) alkylamino, aryl and heteroaryl, and wherein said aryl and heteroaryl groups can optionally be substituented with one or more substituents, preferably from zero to two substutuents, independently selected from halo, oxo, nitro, amino, cyano, (C_1-C_6) alkyl optionally substituted with from one to three fluorine atoms and (C_1-C_6) alkoxy optionally substituted with from one to three fluorine atoms;

R^1 is hydrogen, (C_1-C_4) alkyl optionally substituted with from one to three fluorine atoms, aryl, -C(O)R^6 wherein R^6 is aryl, (C_1-C_4) alkyl, or aryl-(C_1-C_4) alkyl-, and wherein the alkyl moieties of the aryl-(C_1-C_4) alkyl- and heteroaryl-(C_1-C_4) alkyl groups can be optionally substituted with from one to three fluoro atoms, and wherein the aryl and heteroaryl moieties of these groups can optionally be substituted with one or more substituents, preferably with from zero to two substituents, independently selected from halo, nitro, amino, cyano, (C_1-C_6) alkyl optionally substituted with from one to three fluorine atoms and (C_1-C_6) alkoxy optionally substituted with from one to three fluorine atoms;

R^4 and R^5 together represent an olefin optionally terminally substituted by one or two substituents, R^7 and R^8, which are independently selected from the group of substituents set forth above in the definition of R^2 and R^3;

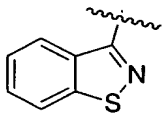
or R^4 and R^5, taken together, can form a spiro saturated ring containing from 3 to 6 carbon atoms, wherein said ring can be optionally substituted by one or two substituents, R^7 and R^8, which are independently selected from the group of substituents set forth above in the definition of R^2 and R^3;

with the proviso that when Ar is benzisothiazol-3-yl, and A is ethylene, and R^1 is hydrogen or unsubstituted (C_1-C_4)alkyl, and R^2 is hydrogen, halo or methyl, and R^3 is hydrogen, halo, nitro, amino, cyano, or

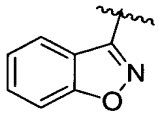
substituted or unsubstituted alkyl or substituted or unsubstituted alkoxy; then R^4 and R^5 cannot form either a spiro (C_4-C_6)cycloalkyl group or an olefin terminally substituted with R^7 and R^8 wherein R^7 is hydrogen and R^8 is phenyl;

or a pharmaceutically acceptable salt of such compound.

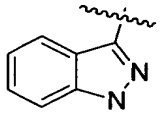
2. A compound according to claim 1 wherein Ar is a substituted or unsubstituted bicyclic ring system selected from the following:



II

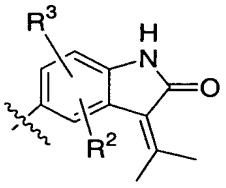


III



IV

and wherein A is $-CH_2-$, $-CH_2-CH_2-$, -(C=O)-, $-CH_2(C=O)-$, -CH(OH)-, $-CH_2-$CH(OH)-, -CH-N(R)-, or $-CH_2-$CH-N(R)-, and wherein the oxindole moiety attached to A is selected from the following:



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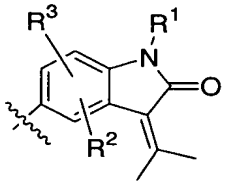

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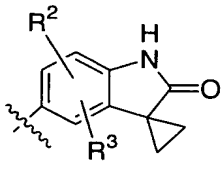
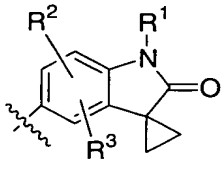


VII



VIII

wherein R^1, R^2 and R^3 are as defined above and wherein the spirocyclopropyl groups can be substituted or unsubstituted.

3. A compound according to claim 1 wherein R^4 and R^5 form a spiro 2,2-dimethylcyclopropyl ring.

4. A compound according to claim 1 wherein R^4 and R^5 form an olefin that is optionally terminally substituted with R^7 and R^8.

5. A compound according to claim 1 that is selected from the following compounds and their pharmaceutically acceptable salts:

5-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-3-isopropylidene-1-methyl-1,3-dihydro-indol-2-one;

5-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-3-isopropylidene-1,3-dihydro-indol-2-one;

5-[3-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-propyl]-3-isopropylidene-1,3-dihydro-indol-2-one;

{5-[3-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-propyl]-3-isopropylidene-2-oxo-2,3-dihydro-indol-1-yl}-acetic acid;

5-[3-(4-1,2-Benzisoxazol-3-yl-piperazin-1-yl)-propyl]-3-isopropylidene-1,3-dihydro-indol-2-one;

5-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-6-chloro-3-isopropylidene-1,3-dihydro-indol-2-one;

5-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-propyl]-6-chloro-3-isopropylidene-1,3-dihydro-indol-2-one;

5-[3-(4-1,2-Benzisoxazol-3-yl-piperazin-1-yl)-ethyl]-3-isopropylidene-1,3-dihydro-indol-2-one;

5-{3-[4-(1H-Indazol-3-yl)-piperazin-1-yl]-propyl}-3-isopropylidene-1,3-dihydro-indol-2-one;

Spiro[cyclopropane-1,3'-{3*H*}indol]-2'(1'*H*)-one,5'-[2-[4-{1,2-benzisothiazol-3-yl}-1-piperazinyl]ethyl]-1',2,2-trimethyl

Spiro[cyclopropane-1,3'-{3*H*}indol]-2'(1'*H*)-one,5'-[2-[4-{1,2-benzisothiazol-3-yl}-1-piperazinyl]ethyl]-2,2-dimethyl-

Spiro[cyclopropane-1,3'-{3*H*}indol]-2'(1'*H*)-one,5'-[3-[4-{1,2-benzisothiazol-3-yl}-1-piperazinyl]propyl]-2,2-dimethyl-

Spiro[cyclopropane-1,3'-{3*H*}indol]-2'(1'*H*)-one,5'-[2-[4-{1,2-benzisothiazol-3-yl}-1-piperazinyl]ethyl]-6'-chloro-2,2-dimethyl-

Spiro[cyclopropane-1,3'-{3*H*}indol]-2'(1'*H*)-one,5'-[3-[4-{1,2-benzisothiazol-3-yl}-1-piperazinyl]propyl]-6'-chloro-2,2-dimethyl-

6. A compound according to claim 1 wherein one or both of R^2 and R^3 are hydrogen.

7. A pharmaceutical composition for treating a disorder or condition selected from single episodic or recurrent major depressive disorders, dysthymic disorders, depressive neurosis and neurotic depression, melancholic depression including anorexia, weight loss, insomnia, early morning waking or psychomotor retardation; atypical depression (or reactive depression) including increased appetite, hypersomnia, psychomotor agitation or irritability, seasonal affective disorder and pediatric depression; bipolar disorders or manic depression, for example, bipolar I disorder, bipolar II disorder and cyclothymic disorder; conduct disorder; disruptive behavior disorder; attention deficit hyperactivity disorder (ADHD); behavioral disturbances associated with mental retardation, autistic disorder, and conduct disorder; anxiety disorders such as panic disorder with or without agoraphobia, agoraphobia without history of panic disorder, specific phobias, for example, specific animal phobias, social anxiety, social phobia, obsessive-compulsive disorder, stress disorders including post-traumatic stress disorder and acute stress disorder, and generalized anxiety disorders; borderline personality disorder; schizophrenia and other psychotic disorders, for example, schizophreniform disorders, schizoaffective disorders, delusional disorders brief psychotic disorders, shared psychotic disorders, psychotic disorders with delusions or hallucinations, psychotic episodes of anxiety, anxiety associated with psychosis, psychotic mood disorders such as severe major depressive disorder; mood disorders associated with psychotic

disorders such as acute mania and depression associated with bipolar disorder; mood disorders associated with schizophrenia; delirium, dementia, and amnestic and other cognitive or neurodegenerative disorders, such as Parkinson's disease (PD), Huntington's disease (HD), Alzheimer's disease, senile dementia, dementia of the Alzheimer's type, memory disorders, loss of executive function, vascular dementia, and other dementias, for example, due to HIV disease, head trauma, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, or due to multiple aetiologies; movement disorders such as akinesias, dyskinesias, including familial paroxysmal dyskinesias, spasticities, Tourette's syndrome, Scott syndrome, PALSYS and akinetic-rigid syndrome; extra-pyramidal movement disorders such as medication-induced movement disorders, for example, neuroleptic-induced Parkinsonism, neuroleptic malignant syndrome, neuroleptic-induced acute dystonia, neuroleptic-induced acute akathisia, neuroleptic-induced tardive dyskinesia and medication-induced postural tremour; chemical dependencies and addictions (*e.g.,* dependencies on, or addictions to, alcohol, heroin, cocaine, benzodiazepines, nicotine, or phenobarbitol) and behavioral addictions such as an addiction to gambling; and ocular disorders such as glaucoma and ischemic retinopathy in a mammal, including a human, comprising an amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, that is effective in treating such disorder or condition, and a pharmaceutically acceptable carrier.

8. A method for treating a disorder or condition selected from single episodic or recurrent major depressive disorders, dysthymic disorders, depressive neurosis and neurotic depression, melancholic depression including anorexia, weight loss, insomnia, early morning waking or psychomotor retardation; atypical depression (or reactive depression) including increased appetite, hypersomnia, psychomotor agitation or irritability, seasonal affective disorder and pediatric depression; bipolar disorders or manic depression, for example, bipolar I disorder, bipolar II

disorder and cyclothymic disorder; conduct disorder; disruptive behavior disorder; attention deficit hyperactivity disorder (ADHD); behavioral disturbances associated with mental retardation, autistic disorder, and conduct disorder; anxiety disorders such as panic disorder with or without agoraphobia, agoraphobia without history of panic disorder, specific phobias, for example, specific animal phobias, social anxiety, social phobia, obsessive-compulsive disorder, stress disorders including post-traumatic stress disorder and acute stress disorder, and generalized anxiety disorders; borderline personality disorder; schizophrenia and other psychotic disorders, for example, schizophreniform disorders, schizoaffective disorders, delusional disorders, brief psychotic disorders, shared psychotic disorders, psychotic disorders with delusions or hallucinations, psychotic episodes of anxiety, anxiety associated with psychosis, psychotic mood disorders such as severe major depressive disorder; mood disorders associated with psychotic disorders such as acute mania and depression associated with bipolar disorder; mood disorders associated with schizophrenia; delirium, dementia, and amnestic and other cognitive or neurodegenerative disorders, such as Parkinson's disease (PD), Huntington's disease (HD), Alzheimer's disease, senile dementia, dementia of the Alzheimer's type, memory disorders, loss of executive function, vascular dementia, and other dementias, for example, due to HIV disease, head trauma, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, or due to multiple aetiologies; movement disorders such as akinesias, dyskinesias, including familial paroxysmal dyskinesias, spasticities, Tourette's syndrome, Scott syndrome, PALSYS and akinetic-rigid syndrome; extra-pyramidal movement disorders such as medication-induced movement disorders, for example, neuroleptic-induced Parkinsonism, neuroleptic malignant syndrome, neuroleptic-induced acute dystonia, neuroleptic-induced acute akathisia, neuroleptic-induced tardive dyskinesia and medication-induced postural tremour; chemical dependencies and addictions (*e.g.*, dependencies on, or addictions to, alcohol, heroin, cocaine, benzodiazepines, nicotine, or phenobarbitol) and behavioral addictions

such as an addiction to gambling; and ocular disorders such as glaucoma and ischemic retinopathy in a mammal, including a human, comprising administering to a mammal in need of such treatment an amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, that is effective in treating such disorder or condition.

9. A method according to claim 8, wherein the disorder or condition that is being treated is selected from major depression, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthymia, cyclothymia and bipolar disorder.

10. A method according to claim 8, wherein the disorder or condition that is being treated is selected from schizophrenia, schizoaffective disorder, delusional disorder, substance-induced psychotic disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, and schizophreniform disorder.

11. A method according to claim 8, wherein the disorder or condition that is being treated is selected from autism, pervasive development disorder, and attention deficit hyperactivity disorder.

12. A method according to claim 8, wherein the disorder or condition that is being treated is selected from generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, and phobias, including social phobia, agoraphobia, and specific phobias.

13. A method according to claim 8, wherein the disorder or condition being treated is schizophrenia with concomitant depression.

14. A method according to claim 8, wherein the disorder or condition being treated is schizophrenia with concomitant anxiety.

15. A method of treating a disorder or condition selected from single episodic or recurrent major depressive disorders, dysthymic disorders, depressive neurosis and neurotic depression, melancholic depression including anorexia, weight loss, insomnia, early morning waking or psychomotor retardation; atypical depression (or reactive depression) including increased appetite, hypersomnia, psychomotor agitation or irritability, seasonal affective disorder and pediatric depression; bipolar disorders or manic depression, for example, bipolar I disorder, bipolar II disorder and cyclothymic disorder; conduct disorder; disruptive behavior disorder; attention deficit hyperactivity disorder (ADHD); behavioral disturbances associated with mental retardation, autistic disorder, and conduct disorder; anxiety disorders such as panic disorder with or without agoraphobia, agoraphobia without history of panic disorder, specific phobias, for example, specific animal phobias, social anxiety, social phobia, obsessive-compulsive disorder, stress disorders including post-traumatic stress disorder and acute stress disorder, and generalized anxiety disorders; borderline personality disorder; schizophrenia and other psychotic disorders, for example, schizophreniform disorders, schizoaffective disorders, delusional disorders, brief psychotic disorders, shared psychotic disorders, psychotic disorders with delusions or hallucinations, psychotic episodes of anxiety, anxiety associated with psychosis, psychotic mood disorders such as severe major depressive disorder; mood disorders associated with psychotic disorders such as acute mania and depression associated with bipolar disorder; mood disorders associated with schizophrenia; delirium, dementia, and amnestic and other cognitive or neurodegenerative disorders, such as Parkinson's disease (PD), Huntington's disease (HD), Alzheimer's disease, senile dementia, dementia of the Alzheimer's type, memory disorders, loss of executive function, vascular dementia, and other dementias, for example, due to HIV disease, head trauma, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, or due to multiple aetiologies; movement disorders such as akinesias, dyskinesias, including familial paroxysmal dyskinesias, spasticities, Tourette's syndrome, Scott

syndrome, PALSYS and akinetic-rigid syndrome; extra-pyramidal movement disorders such as medication-induced movement disorders, for example, neuroleptic-induced Parkinsonism, neuroleptic malignant syndrome, neuroleptic-induced acute dystonia, neuroleptic-induced acute akathisia, neuroleptic-induced tardive dyskinesia and medication-induced postural tremour; chemical dependencies and addictions (*e.g.,* dependencies on, or addictions to, alcohol, heroin, cocaine, benzodiazepines, nicotine, or phenobarbitol) and behavioral addictions such as an addiction to gambling; and ocular disorders such as glaucoma and ischemic retinopathy in a mammal, including a human, comprising administering to said mammal:

(a) a compound according to claim 1 or a pharmaceutically acceptable salt thereof; and

(b) another pharmaceutically active compound that is an antidepressant or an anti-anxiety agent, or a pharmaceutically acceptable salt thereof;

wherein the active agents "a" and "b" are present in amounts that render the combination effective in treating such disorder or condition.